Normal patterns and pitfalls of FDG uptake in the head and neck

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Abstract:

In order to avoid misdiagnoses, medical imagers should be familiar with the normal patterns and distribution of FDG activity within the head and neck, as well as the pathophysiology and imaging-findings of common diagnostic pitfalls related to incidental FDG-avid lesions. The purpose of this article is to provide an image-rich review of the normal patterns of FDG uptake in the head and neck, help differentiate benign from malignant incidentally found FDG-avid foci, and detail important “don’t miss” hypometabolic head and neck lesions on PET/CT and PET/MRI.

Key Words:

FDG, PET/CT, PET/MRI, radiotracer distribution, benign, malignant, pitfalls

Introduction:

Positron emission tomography/computed tomography (PET/CT) and, more recently, positron emission tomography-magnetic resonance imaging (PET/MRI) with fluorine-18-fluorodeoxyglucose (^{18}F-FDG) are vital imaging modalities for the evaluation of numerous and histopathologically-varied neoplasms within the head and neck.[1-3] An invaluable tool throughout the process of managing oncologic conditions, ^{18}F-FDG PET/CT is regularly utilized in head and neck cancer imaging for the detection, initial diagnosis, and staging of tumors, evaluation of treatment response, monitoring for recurrence, and long-term surveillance.[2,4,5] A newer technology, ^{18}F-FDG PET/MRI is less established in the evaluation of head and neck cancer, but has shown promise given its superior tissue contrast resolution, lower ionizing radiation dose, and superior assessment of perineural tumor spread.

Despite their tremendous utility, the accurate interpretation of ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI requires comprehensive awareness and familiarity with many diagnostic challenges and pitfalls.[6-10] Owing to the detailed and challenging anatomy of the region, as well confounding factors related to prior surgery and radiation, this requirement is only magnified with head and neck oncologic imaging.[6,7,10] The purpose of this article is to provide a review of the normal patterns of ^{18}F-FDG uptake in the head and neck, as well as imaging findings of common diagnostic pitfalls related to false-negative exams and incidentally found ^{18}F-FDG -avid foci in the head and neck on PET/CT and PET/MRI.

Basics of FDG Physiology and Imaging:

Though a detailed exposition of the physiology, physics, and specific protocols for ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI would far exceed the scope of this article, a brief preliminary discussion of the modality's core elements is necessary for understanding its common interpretive pitfalls. The utility of PET in the evaluation of malignant tumors is premised on altered glucose metabolism.[1,3,11] In order to meet their energy requirements, metabolically active tumor cells depend on glycolysis, which is promoted by the activation of the hexose monophosphate pathway and the upregulated expression of glucose transporter proteins and hexokinase within malignant cells.[1,3,11] As an analog of glucose, intravenously administered ^{18}F-FDG is taken up by tumor cells via glucose transporter proteins and phosphorylated by hexokinase.[1,11] However, unlike glucose-6-phophate, once phosphorylated, ^{18}F-FDG does not undergo further metabolism in the glycolytic pathway.[11] Rather, the phosphorylated ^{18}F-FDG persistently accumulates[1] and, due to the lack of requisite amount of glucose-6-phosphatase, remains trapped intracellularly within tumor cells.[3,11] Consequently, ^{18}F-FDG serves as a useful representation of the degree of glucose uptake throughout the body when the patient is subsequently imaged.[3]

To allow for an appropriate degree of ^{18}F-FDG uptake, imaging of the patient is typically performed approximately 60 – 90 minutes after 5 - 15 mCi (175 – 550 MBq) of ^{18}F-FDG have been administered intravenously.[12] Whole-body CT was first employed in conjunction with PET imaging primarily to supplement the modality by providing anatomic correlation and localization of molecular data and to enhance photon attenuation correction.[2,6,11-13] However, with improved technologies and imaging techniques, PET imaging is now frequently combined not only with low-dose and/or

noncontrast CT but high-resolution, diagnostic-quality CT imaging or magnetic resonance imaging.[5,14] The concurrent acquisition of high-resolution CT imaging or MRI often obviates the need for obtaining separate diagnostic-quality imaging,[5] which is paramount in head and neck oncology for accurate staging and surgical planning.

PET/CT and PET/MRI Imaging Pitfalls:

While the increased utilization of hybrid ^{18}F-FDG PET/CT has significantly improved the characterization of primary head and neck malignancies and the identification of locoregional and metastatic disease, accurate interpretation of the combined modality necessitates that imagers are familiar with its common imaging pitfalls. Most commonly, challenges and pitfalls in oncologic head and neck PET/CT or PET/MRI are related to physiologic uptake of ^{18}F-FDG, incidental foci of increased ^{18}F-FDG uptake, and false-negative non-FDG avid lesions.[6-10,15] Frequently encountered examples of physiologic ^{18}F-FDG uptake include metabolic activity associated with normal lymphoid tissue, brown fat, thyroid and salivary gland tissue, and muscle activity.[6-10,16] Incidental foci of increased ^{18}F-FDG uptake can also be seen with vocal cord paralysis, incidental thyroid and salivary gland lesions, and infectious or inflammatory processes.[6-10,16] Though less common, false-negative lesions may not be accurately characterized or missed due to location of the lesion and neoplastic characteristics, such as histopathologic type and tumor size and degree of necrosis.[5-10,12]

Incidental FDG Uptake

Thyroid Gland Uptake

On ^{18}F-FDG PET imaging, the thyroid gland demonstrates variable ^{18}F-FDG uptake and, due to incidental focal or diffusely increased metabolic activity, can present pitfalls for head and neck oncologic PET/CT or PET/MRI.[7,10,15,17] Typically, physiologic ^{18}F-FDG uptake within the thyroid gland is either absent or minimal and homogeneous in distribution.[16-18] Additional patterns of ^{18}F-FDG uptake within the thyroid gland include symmetric diffusely increased uptake and focal increased uptake, which can both be seen with physiologic, benign, and pathological conditions.[6,7,10,19] Diffuse symmetric uptake of ^{18}F-FDG within the thyroid gland usually represents either physiologic uptake or a benign etiology, such as multinodular goiter, Grave disease, or chronic autoimmune thyroiditis.[7,10,17,19] (Figure 1)

When focal ^{18}F-FDG uptake within the region of the thyroid gland is identified on PET, it is important that the corresponding CT or MR images are carefully scrutinized, as the uptake can be mistakenly attributed to adjacent cervical nodal uptake.[10,16,20] Focal ^{18}F-FDG uptake within the thyroid gland is nonspecific and can be seen with benign conditions, such as a thyroid adenoma, or in the setting of thyroid malignancy.[6,7,10] The precise risk of malignancy in lesions with focal thyroid ^{18}F-FDG uptake is equivocal with reported risk of malignancy ranging from 25-63%.[10,18,21,22] As a result, it is recommended that foci of moderate to high ^{18}F-FDG uptake undergo further diagnostic evaluation with thyroid ultrasound and/or fine-needle aspiration biopsy.[6,7,10,18] (Figure 2)

Salivary Gland Uptake

^{18}F-FDG is normally taken up physiologically by the salivary glands and subsequently excreted through the saliva.[7,10] Accordingly, the parotid and submandibular glands usually demonstrate symmetric low to moderate ^{18}F-FDG uptake,[7,10,16] however the glands may occasionally demonstrate minimal or no uptake.[7] The normal physiologic uptake within the parotid and submandibular glands can both simulate and obscure salivary gland tumors.[23] Additional patterns of ^{18}F-FDG uptake within the salivary glands include diffusely increased uptake and asymmetric or focal increased uptake, which may present additional challenges to those interpreting PET/CT and PET/MRI of the head and neck.[7,10]

There are a number of benign, non-neoplastic conditions that can result in increased ^{18}F-FDG uptake within the salivary glands.[7,10] For example, infectious etiologies, such as viral, bacterial, and tuberculous infections, radiation-induced sialadenitis, obstructive/calculous sialadenitis, and inflammatory conditions, such as sarcoidosis, can cause increased uptake within the salivary glands.[6,7,10,24] (Figure 3) Asymmetric uptake can also be observed secondary to compensatory hypertrophy following contralateral gland resection.[7,10]

In addition to non-neoplastic etiologies, salivary gland tumors can demonstrate increased ^{18}F-FDG uptake, which is usually asymmetric and focal.[6,7,10,23,25] (Figure 4) While high-grade tumors in the salivary gland tend to have higher ^{18}F-FDG uptake than those of low or intermediate-grade,[23] there are benign parotid gland tumors, such as papillary cystadenoma lymphomatosum (Warthin tumor) and pleomorphic adenoma (benign mixed tumor), which can also demonstrate increased uptake.[6,7,10,23] Additionally, it is important to note that some malignant salivary gland tumors may not

demonstrate significantly elevated ^{18}F-FDG uptake, including low grade mucoepidermoid and adenoid cystic carcinomas.[7,10,23] Thus, the lack of significant uptake within a salivary gland lesion does not exclude a malignant etiology.[7] Due to the lack of definitive differentiation of benignity versus malignancy based on ^{18}F-FDG uptake, focal asymmetric salivary gland uptake always requires careful evaluation of the associated CT or MRI component of the examination, as well as correlation with pertinent patient history.[7] Additional imaging, such as ultrasound or high-resolution MRI may be complementary in better delineating lesion margins (circumscribed margins suggest a benign tumor or low grade malignancy; infiltrating margins suggest a high grade malignancy) and assessing lesion cellularity (low T2 or ADC signal intensity on MRI suggests a cellular tumor that is more likely to be malignant), but definitive diagnosis requires imaging-guided biopsy or surgical resection.[10,25]

Brown Fat

Within the human body, there are two morphologically and functionally distinct types of adipose tissue: white adipose tissue (WAT) and brown adipose tissue (BAT).[26] White adipose tissue has relatively low-level metabolic activity and primarily functions to provide energy storage and insulation.[27-29] However, more than displaying these relatively inert characteristics, white adipose tissue, in so far as it secretes important hormones and cytokines and plays an important role in insulin resistance and inflammation, is now understood to also function as an endocrine organ.[26,30] Brown adipose tissue, while also storing energy,[26] mainly serves to produce heat, which can occur in the setting of cold temperatures (non-shivering thermogenesis) or following

food intake (diet-induced thermogenesis).[26,28,29] In addition to its high vascularity, considerable sympathetic noradrenergic innervation, and adrenergic receptor expression, brown adipose tissue expresses a mitochondrial uncoupling protein.[27-29] This protein facilitates uncoupling of oxidative phosphorylation within mitochondria, which results in the direct production of heat instead of utilizing adenosine triphosphate (ATP).[27-29] These physiologic processes have important implications, due to the resulting intense FDG uptake within brown adipose tissue on PET/CT and PET/MRI.[10,27,31]

Typically, brown adipose tissue appears on ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI as symmetric, fusiform-shaped, curvilinear foci of FDG uptake that correspond to areas of fat density (approximately -100 CT units) on CT images or fat signal intensity (T1 and T2 bright) on MR images.[7,10,29] (Figure 5) BAT can be found in the axillae, intercostal spaces, and para-aortic and perinephric regions of the abdomen.[29] However, most commonly and of critical importance for head and neck cancer imaging, brown adipose tissue is located within the deep cervical neck and supraclavicular regions.[10,28,29] Though the precise demographics, including prevalence, and the factors contributing to the presence of brown adipose tissue on ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI remain uncertain, BAT has been observed within the head and neck in approximately 2.5- 4.0% of imaged patients and has been overall more frequently observed in children,[32] women, and during the winter months.[31] Corresponding to the physiology of brown adipose tissue, proposed mechanisms to reduce ^{18}F-FDG activity within BAT includes increasing ambient room temperature, application of warm

blankets, and the administration of medications prior to imaging, such as propranolol, diazepam, and fentanyl.[7,29,31,32]

Muscle Uptake

Due to the number and small size of muscles within the head and neck, physiologic muscle uptake of ^{18}F-FDG represents an additional challenge for oncologic imaging of the head and neck.[16] Physiologic muscle uptake of ^{18}F-FDG can be observed with involuntary muscle activity (Figure 6), voluntary muscle activity (Figure 7), and in response to insulin administration or recent food ingestion.[33] For example, focal uptake within the extraocular muscles can occur secondary to eye motion.[10,16] With talking and phonation, ^{18}F-FDG uptake may commonly be seen within the genioglossus, cricopharyngeus, and posterior cricoarytenoid muscles.[10] Physiologic uptake associated with masseteric activity may also be seen with talking or chewing.[33] Besides ^{18}F-FDG uptake within particular muscle groups, diffuse skeletal uptake can also occur secondary to voluntary activity related to recent strenuous exercise.[33]

In addition to uptake associated with these voluntary activities, ^{18}F-FDG uptake is frequently observed within the sternocleidomastoid, longus colli, anterior scalene, longus capitis, and obliquus capitis inferior muscles due to anxiety associated muscle contraction.[7,9,10,16,33,34] Similarly, scalene and sternocleidomastoid muscle uptake can be also be seen with coughing or labored breathing.[33] In addition, if the patient is imaged following the administration of insulin or in the postprandial state, the patient may exhibit diffuse ^{18}F-FDG skeletal muscle uptake.[33,35]

On ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI, muscle uptake is reliably distinguished by mild to moderate symmetric and linear ^{18}F-FDG uptake that can be followed on corresponding CT or MR images from the insertion of the muscle to its origin.[6,10,35] The linearity may not always be evident on axial images and scrutinizing the coronal and sagittal reconstructed CT or acquired multiplanar MR images is helpful to demonstrate the typically linear configuration of uptake within the muscle or muscle group. In order to avoid the challenges associated with physiologic muscle uptake, certain preventative measures ought to be taken prior to imaging. The patient should be asked to fast for at least 4-6 hours[35] and to refrain from intense exercise for at least 24[35] to 48[33] hours prior imaging. Additionally, during the uptake component of the PET/CT of PET/MRI examination after ^{18}F-FDG has been administered, the patient should be asked to remain as calm and relaxed as possible and to avoid any muscle activity, such as talking, chewing, or performing other physical activities that might promote FDG uptake.[6,10,33,35] In order to help reduce anxiety-related muscle uptake, benzodiazepine administration prior to the examination can also be considered.[10,35,36]

Vocal Cord Paralysis

Occasionally, asymmetric ^{18}F-FDG uptake within the vocal cords can present a diagnostic challenge on PET/CT or PET/MRI. Asymmetric ^{18}F-FDG vocal cord uptake often occurs in the setting of unilateral vagus or recurrent laryngeal nerve injury, which may occur secondary to involvement of the nerve by a tumor or injury from prior surgery or trauma.[7,10,37] In order to offset the paralysis of the affected vocal cord, the functioning, non-paralyzed contralateral vocal cord demonstrates compensatory

increased activity during phonation.[7,10,37] (Figure 8) This heightened activity results in corresponding increased metabolism and glucose, particularly within the thyroarytenoid and posterior circoarytenoid muscles.[10,38] It is imperative to scrutinize the associated anatomic CT or MR images through the level of the vocal cords, as focal uptake can simulate a lesion within the normal vocal cord.[7,10]

On the PET component of PET/CT or PET/MRI, vocal cord paralysis, as a result of the compensatory increased activity and associated heightened metabolism and glucose uptake, results in focal avid ^{18}F-FDG uptake within the non-paralyzed vocal cord.[7,10,33,37] If asymmetric focal uptake is identified within a vocal cord, inspection of the contralateral vocal cord should be performed to assess for common imaging findings of paralysis or dysfunction. These findings typically include a paramedian location of the paralyzed vocal cord, dilated ipsilateral laryngeal ventricle ("Spinnaker sail" sign),[39] medialized and thickened ipsilateral aryepiglottic fold, dilated ipsilateral pyriform sinus, and, possibly, posterior cricoarytenoid and thyroarytenoid muscle atrophy.[10,39-41]

In addition to the characteristic imaging features on CT of vocal cord paralysis, focal ^{18}F-FDG uptake within the vocal cord should also be correlated with available pertinent patient clinical information.[10] History and physical examination findings of hoarseness and a documented history of previous radiation or surgery to the neck or mediastinum may corroborate and explain observed imaging findings.[10,41] Additionally, as vocal cord paralysis can be caused by disease occurring at any location from the brainstem to the distal aspect of the recurrent laryngeal nerves, it is imperative that the expected course of the involved vagus (jugular foramen and carotid space) and recurrent laryngeal nerves (tracheoesophageal groove bilaterally, aortopulmonary

window on the left, and below subclavian artery on the right) are inspected on CT or MR images to evaluate for contributing pathology.[39-41]

Lymphoid Tissue and Inflammatory Processes

Focal increased ^{18}F-FDG uptake within the head and neck on PET/CT or PET/MRI, which can potentially simulate a neoplastic process, is commonly encountered as result of physiological uptake within lymphoid tissue.[6,7,9,16] The tissues of the head and neck are abound with lymphatic structures, including lymphatic channels, lymph nodes, and the nasopharyngeal (adenoid), palatine, and base of tongue (lingual) tonsillar tissue of the Waldeyer ring.[6-8,10,16] Physiologic uptake within lymphoid tissue, which occurs secondary to the accumulation of ^{18}F-FDG within lymphocytes and macrophages, can symmetric or asymmetric.[6,7,10] Unfortunately, the pattern of uptake is not always helpful as symmetric uptake, though generally reassuring, can occasionally be seen with malignancy, such as in extra-nodal non-Hogkin lymphoma and squamous cell carcinoma.[6,10] Similarly, focal asymmetric uptake does not necessarily imply malignancy and can be seen with be seen with benign variant physiological uptake.[6,7,10] In attempting to decipher benign from malignant etiologies on PET/CT or PET/MRI, it is imperative that the CT or MR images are carefully inspected for corresponding abnormalities, such as the presence of a mass lesion, morphological asymmetry, and loss of fat planes with infiltration of adjacent spaces and structures.[10] Ultimately, equivocal findings require correlation with patient history and clinical evaluation, including endoscopy.[10]

In addition to physiological uptake within lymphoid tissue, there are numerous benign infectious, inflammatory, and granulomatous conditions that, as a result of increased glycolysis within macrophages, also commonly demonstrate focal ^{18}F-FDG uptake and can mimic head and neck malignancy.[6-8,10] Owing to chemotherapy-associated immunosuppression, focal uptake at sites of infection or within reactive lymph nodes is frequently encountered with ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI of head and neck malignancies.[6,9] Similarly, focal ^{18}F-FDG uptake is commonly seen with indwelling ports and catheters.[6,10,42] Additional etiologies for inflammatory associated focal uptake within the head and neck include vasculitides, foreign body granulomas, and active atherosclerotic plaque.[6,10] With active atherosclerotic plaque, ^{18}F-FDG accumulates within plaque associated inflammatory cells, and the degree of uptake appears to correspond to the severity of vessel wall inflammation.[6,10,43] (Figure 9)

The interpretation of ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI of head and neck malignancy is further complicated by the imaging pitfalls associated with postsurgical and recent radiation inflammatory changes.[6,8-10] As a result of tissue injury, surgery generates an inflammatory response[8,42] with the ensuing development of edema, granulation tissue, and scarring.[10] The inflammatory process may have associated elevated ^{18}F-FDG uptake, which, in addition to postsurgical anatomic changes on CT, can make evaluation on PET/CT or PET/MRI examinations performed after surgery challenging.[6,8,10] As the uptake associated with postsurgical inflammatory changes steadily decreases over the few weeks after surgery, the first postoperative ^{18}F-FDG PET/CT or ^{18}F-FDG PET/MRI should optimally be delayed 4-6 weeks after surgery to avoid false-positive imaging findings.[6,10] Similarly, while ^{18}F-FDG PET/CT has shown to

be of significant utility in the evaluation of head and neck tumor recurrence,[5,10] the focal ^{18}F-FDG uptake associated with postradiation inflammatory changes within the field of radiation can simulate residual tumor or recurrence.[4,6,10,12] Though the ideal timing remains uncertain and controversial,[8] the first ^{18}F-FDG PET/CT or ^{18}F-FDG PET/MRI performed after radiation ought to be delayed at least 2-3 months to hopefully allow for resolution of the inflammatory changes and associated false-positive PET imaging findings.[10]

Common False Negatives:

In addition to incidental ^{18}F-FDG uptake, imagers must be aware of the frequently encountered causes of false-negative head and neck ^{18}F-FDG PET/CT or ^{18}F-FDG PET/MRI examinations. Most commonly, false-negative studies within the head and neck are due to concerning lesions that may not demonstrate significant ^{18}F-FDG uptake. There are a number of factors that may contribute to the observed lack of significant ^{18}F-FDG uptake within tumors of the head and neck, including prior treatment, the tumor's location, histopathological type, size, and degree of tumor necrosis.[5,8,10,12] For example, false-negative results can be seen when tumors are located within areas that closely approximate tissues that have high physiologic ^{18}F-FDG uptake, such as lesions in or near the skull base that are close to the brain or tumors within the oral cavity that are near tonsillar tissue.[6,10] Additionally, head and neck tumors or lymph nodes that are small in size (approximately 5-8 mm),[12] can be missed or misinterpreted due to limitations of PET spatial resolution and partial volume effect.[6,8,10,12]

Besides a tumor's size and location, false-negative results on head and neck ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI can be seen due to the particular histopathology type and degree of necrosis. Some types of malignancy that are commonly seen or can occur within the head and neck, such as well-differentiated thyroid cancer, adenoid cystic and mucoepidermoid salivary gland tumors, and spindle cell tumors, may demonstrate low ^{18}F-FDG uptake, consequently producing false-negative findings.[8,10] Further, if the tumor or lymph node has significant necrosis, the lesion may demonstrate falsely-negative absent or low ^{18}F-FDG uptake due to the lack of requisite metabolically active tissue.[5,8,10] (Figure 10) Lastly, false-negative results on head and neck ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI can also be observed on post-treatment imaging studies. While recent radiation and surgery are common causes of false-positive findings within the head and neck,[6,8-10] radiation and chemotherapy can also contribute to false-negative results.[6] If imaging is performed too early following the completion of radiation or chemotherapy, falsely-negative absent or low ^{18}F-FDG uptake within the tumor may be observed due to altered kinetics of ^{18}F-FDG uptake.[6,12]

In addition to low uptake, false-negative head and neck ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI examinations can occur due to misleading symmetric ^{18}F-FDG accumulation within potentially concerning lesions. While most malignancies within the head and neck demonstrate asymmetric ^{18}F-FDG uptake, some malignancies may manifest bilateral disease or may demonstrate metabolic symmetricity. For example, squamous cell carcinomas of the tongue base or nasopharynx may demonstrate bilateral ^{18}F-FDG uptake.[10] These instances of symmetric and bilateral ^{18}F-FDG uptake emphasize the importance of carefully evaluating the CT and MR images for the

presence of associated suspicious findings, such as a mass lesion or the loss of normal fat planes.[10]

Conclusions:

^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI are essential tools for oncologic imaging and of tremendous utility in the diagnosis and staging of head and neck cancer. However, the accurate interpretation of these modalities necessitates that head and neck imagers are cognizant of the many diagnostic challenges and pitfalls commonly found within the head and neck on ^{18}F-FDG PET/CT and ^{18}F-FDG PET/MRI. In order to avoid misdiagnosis, imagers should be familiar with the pathophysiology and normal patterns of ^{18}F-FDG uptake within the head and neck, common false-negative (non-FDG avid) lesions, and troubleshooting of incidental foci of ^{18}F-FDG uptake. Moreover, head and neck imagers should be aware of the appropriate recommendations to provide referring clinicians when imaging pitfalls and challenges are encountered.

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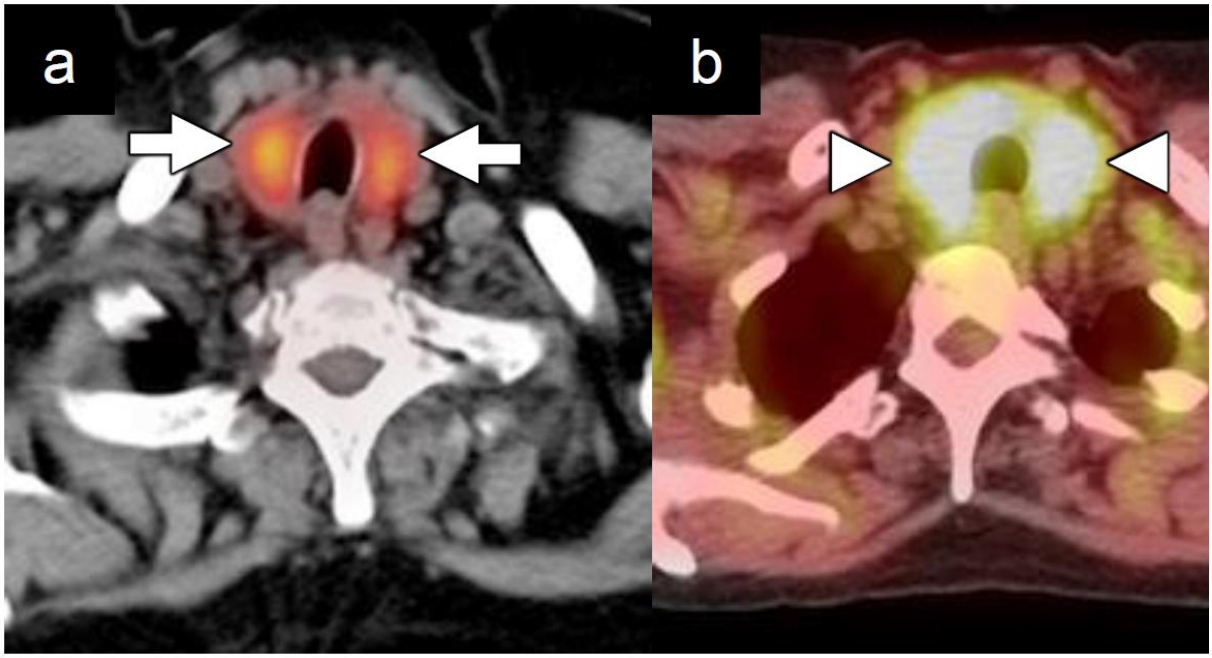

Figure 1. Incidental symmetric, diffusely increased thyroid FDG uptake. Fused axial FDG-PET/CT (a) in a patient with Hodgkin lymphoma demonstrates diffuse mildly increased thyroid gland FDG uptake (white arrows). The patient's history and laboratory values were compatible with subclinical hypothyroidism. Fused axial FDG-PET/CT (b) in different patient with a history of Hodgkin lymphoma demonstrates significant diffuse thyroid gland uptake (white arrowheads). The patient's history and laboratory values were also compatible with hypothyroidism.

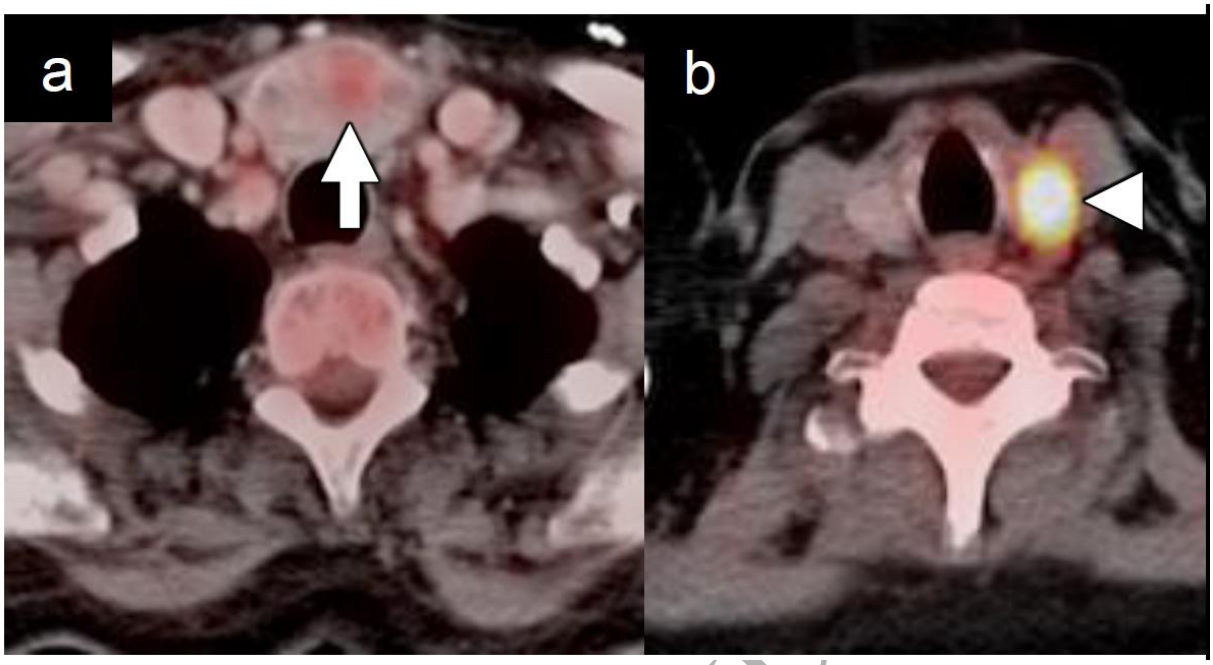

Figure 2. Incidental focal thyroid FDG uptake. Fused axial FDG-PET/CT (a) demonstrates an enlarged thyroid gland with a small focus of mildly increased uptake within the left mid gland (white arrow) in a patient with a history of squamous cell carcinoma of the right maxilla presenting for initial staging. Ultrasound guided biopsy of the lesion was performed with pathology demonstrating benign thyroid nodule. Fused axial FDG-PET/CT (b) shows a focus of markedly increased uptake within the left lobe of the thyroid (white arrowhead) in a patient with a history of breast cancer status post lumpectomy and chemotherapy presenting for restaging. Ultrasound guided biopsy of the lesion was performed with pathology demonstrating follicular neoplasm. However, the lesion was subsequently resected with pathology demonstrating benign follicular nodule.

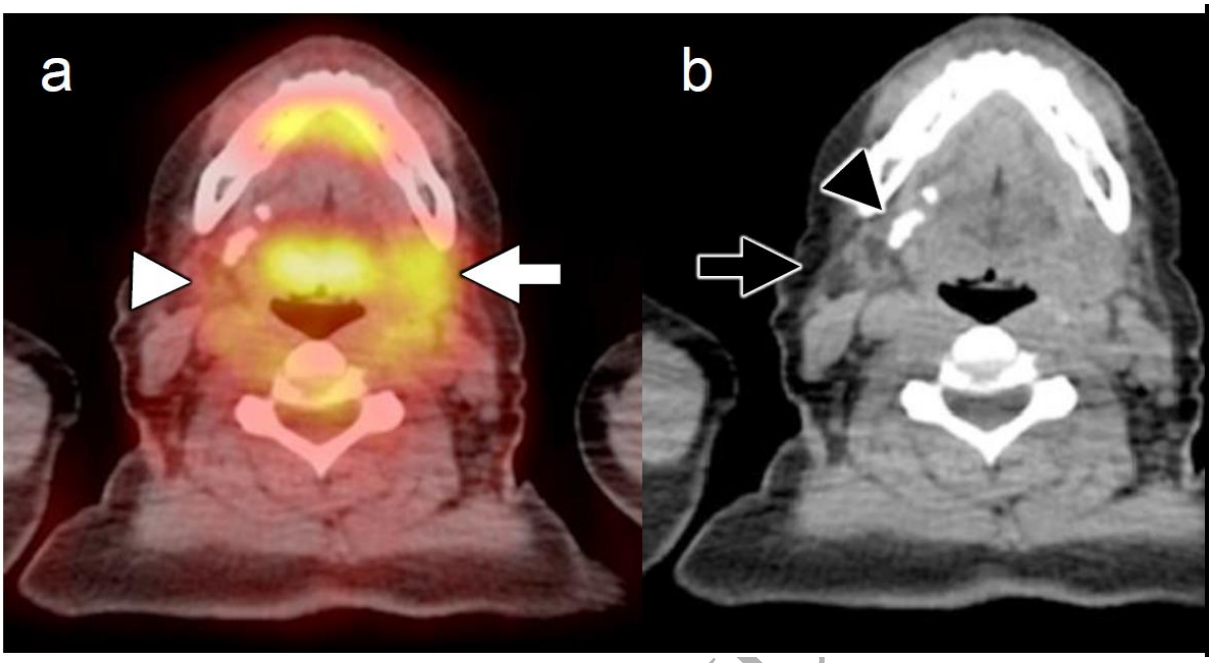

Figure 3. Asymmetric submandibular gland FDG uptake. Fused axial FDG-PET/CT (a) demonstrates asymmetric increased FDG uptake within the left submandibular gland (white arrow) relative to the right submandibular gland (white arrowhead). Axial NECT image in the same patient shows fatty atrophy of the right submandibular gland (black arrow) with associated large ductal calcifications (black arrowhead) from sialoliths that have chronically obstructed the submandibular duct. The left submandibular shows compensatory enlargement, but is otherwise normal in appearance.

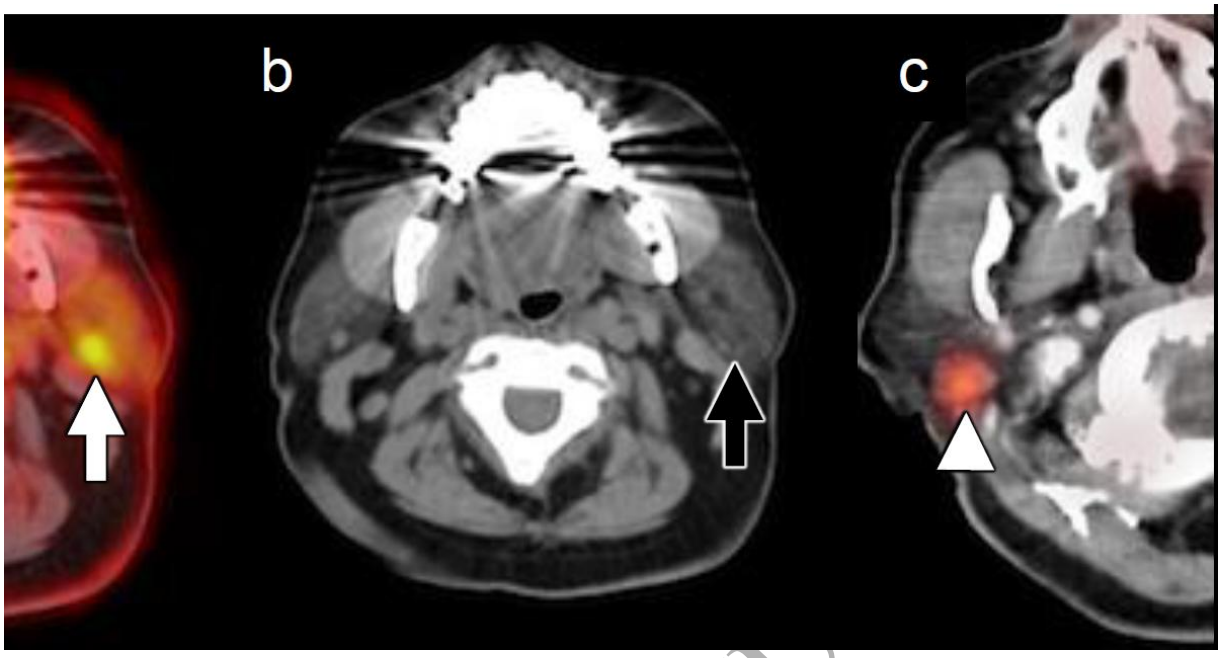

Figure 4. Focal salivary gland FDG uptake. Fused axial FDG-PET/CT (a) shows a small focus of increased FDG uptake within the left superficial parotid gland (white arrowhead). Axial CECT (b) in the same patient shows a subtle idodense/isoenhancing nodule (black arrow) in the superficial parotid. Ultrasound-guided biopsy demonstrated poorly differentiated carcinoma. (c) Fused axial FDG-PET/CT (c) in a different patient with breast cancer presenting for initial staging demonstrates a small FDG avid mass within the right superficial parotid gland (white arrowhead). Axial CECT of the same patient (d) shows a corresponding enhancing mass within the right parotid gland (black arrowhead) corresponding to the focus of increased FDG uptake. Ultrasound-guided biopsy of the lesion demonstrated pleomorphic adenoma.

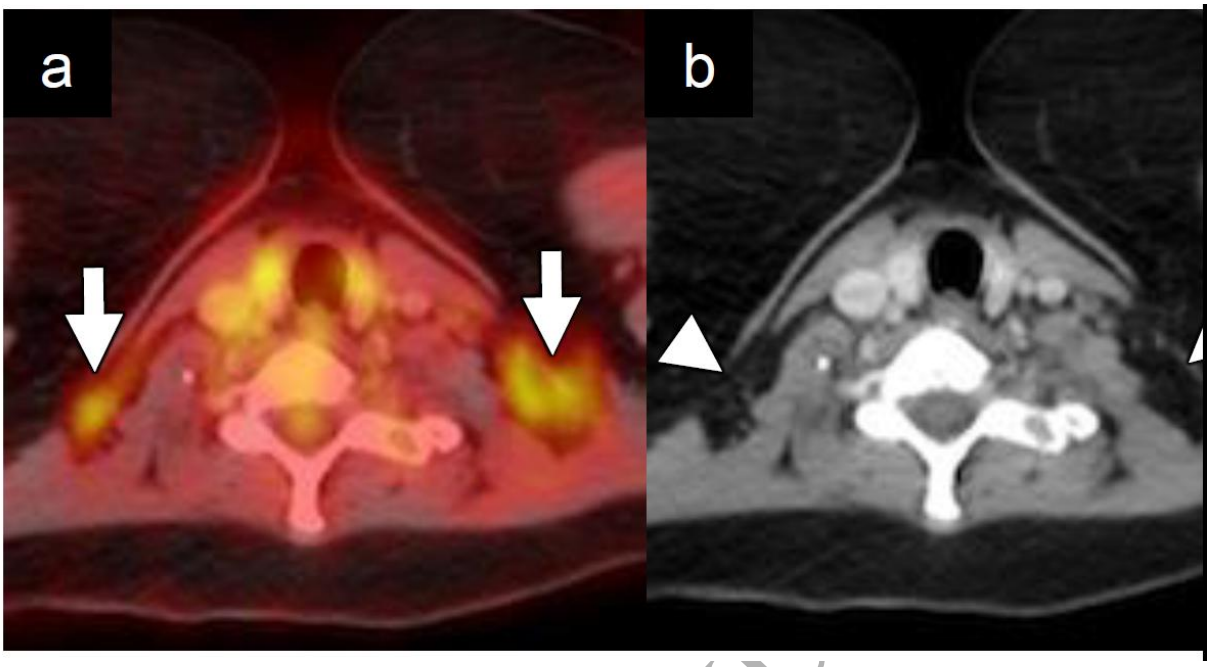

Figure 5. FDG uptake in brown adipose tissue. Fused axial FDG-PET/CT (a) shows bilateral focal FDG uptake within the supraclavicular regions (white arrows). Corresponding axial CECT image shows fat density (white arrowheads) corresponding to areas of uptake on FDG/PET, diagnostic of brown fat.

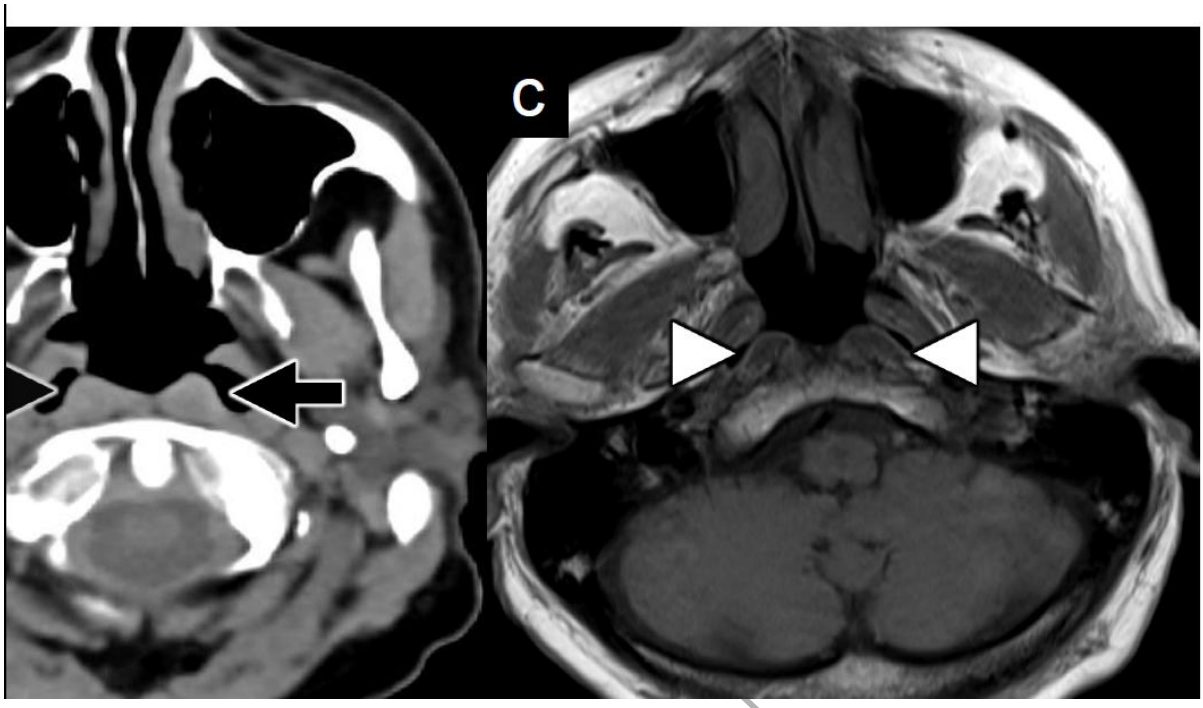

Figure 6. Involuntary muscular activity with FDG uptake. Fused axial PET/CT (a) shows symmetric increased FDG uptake along the posterior wall of the nasopharynx (white arrows). Axial NECT (b) shows corresponding normal appearance of the longus colli (black arrows), which is confirmed on (c) axial T1-weighted MRI (white arrowheads).

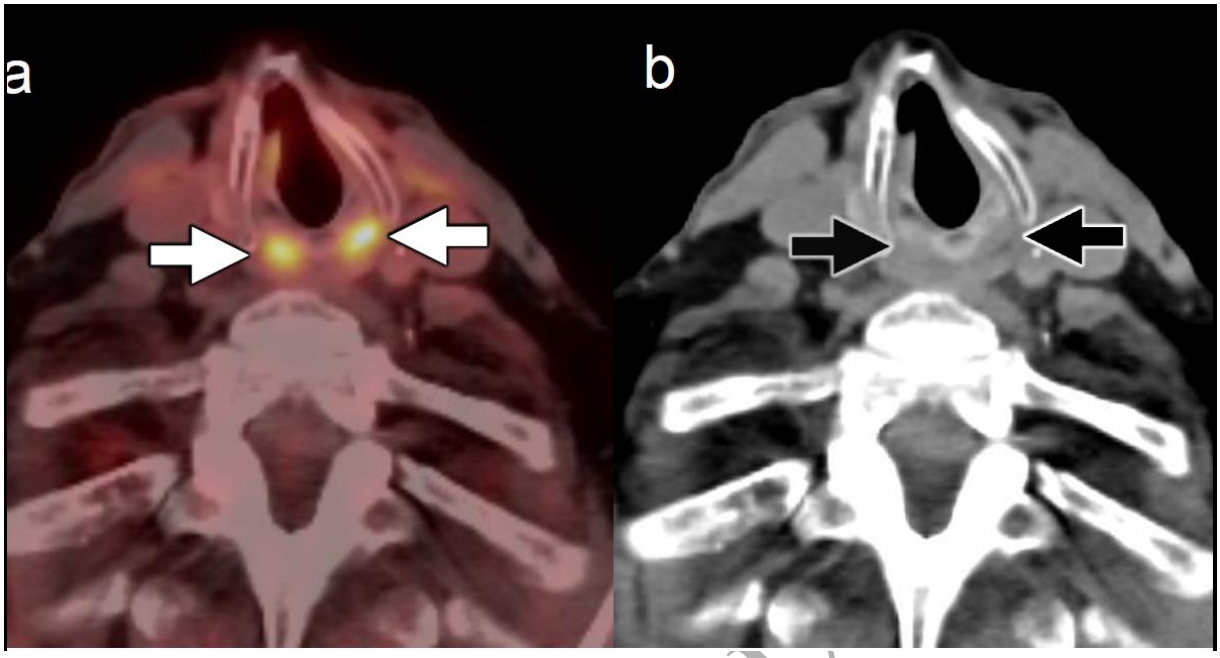

Figure 7. Voluntary muscular activity with FDG uptake. Fused axial PET/CT (a) shows bilateral FDG avidity (white arrows) posterior to the cricoid. Axial NECT (b) shows normal appearance of the postcricoid region bilaterally (black arrows), confirming that the FDG uptake was related to phonation activity involving the posterior cricoarytenoid muscles.

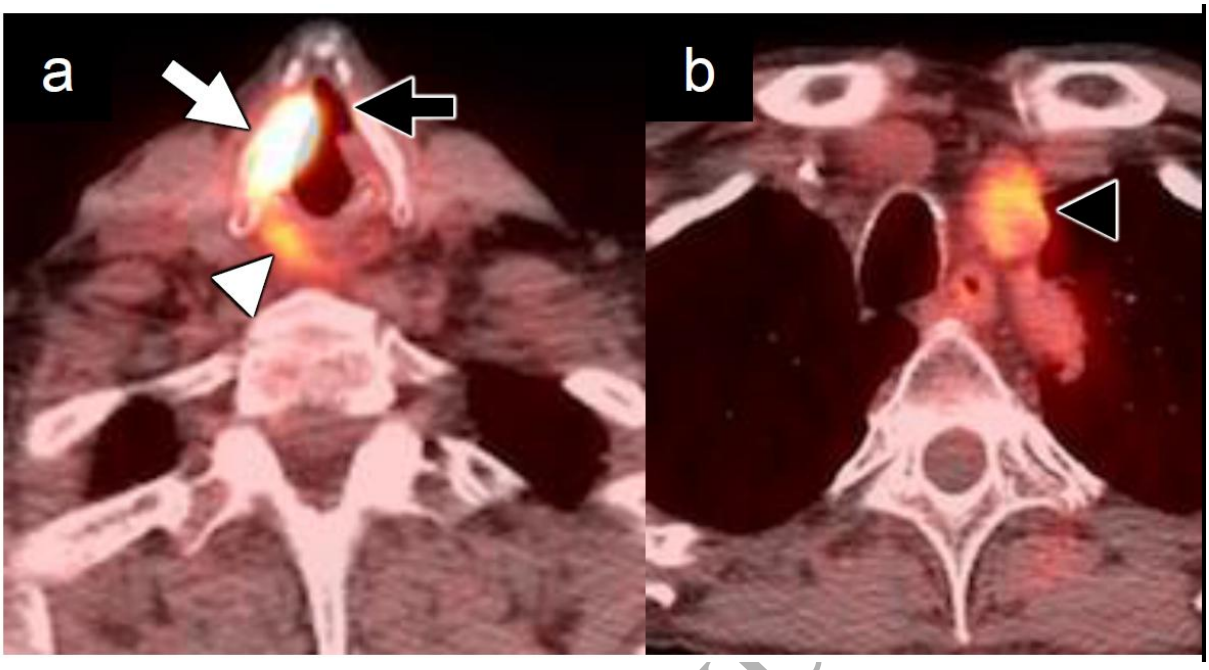

Figure 8. Asymmetric FDG uptake due to left-sided vocal cord paralysis. Fused axial FDG-PET/CT (a) shows the normally functioning right vocal cord (white arrow) with dramatically increased FDG uptake compared to the paralyzed left vocal cord. Note additional dilatation of the left laryngeal ventricle (black arrow) resulting in a “spinnaker sail” sign, as well as asymmetrically increased FDG uptake in the functional right posterior cricoarytenoid muscle (white arrowhead). Fused axial FDG-PET/CT at the level of the clavicles (b) shows a causative FDG avid metastatic lymph node (black arrowhead) that involved either the vagus or recurrent laryngeal nerve.

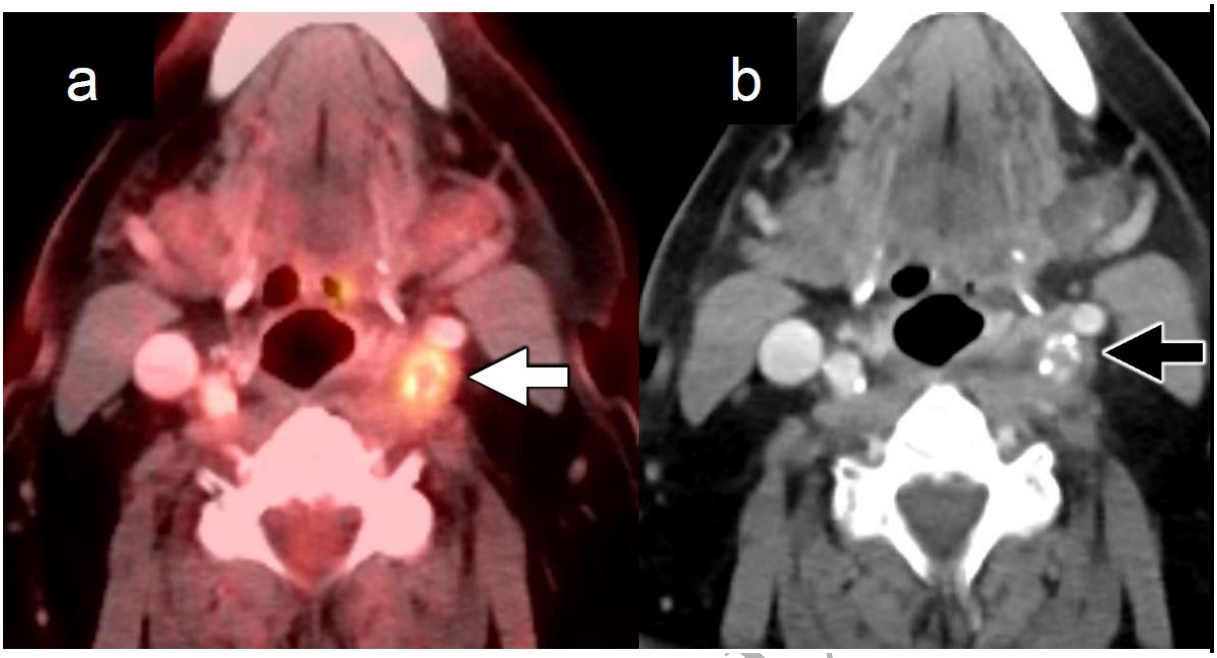

Figure 9. FDG uptake due to atherosclerosis. Fused axial FDG-PET/CT (a) in a patient with esophageal adenocarcinoma shows an isolated focus of hypermetabolic activity within the left suprahyoid neck (white arrow). A metastatic level II lymph node would be an unusual location for an isolated metastasis from esophageal carcinoma. Corresponding axial CECT (b) demonstrates that the area of uptake corresponds to the left internal carotid artery (black arrow) not a cervical chain lymph node. Note a “rim” sign of adventitial calcification, as well as eccentric soft tissue component in this patient with active inflammation from atherosclerotic disease with high-risk plaque ulceration and likely intraplaque hemorrhage.

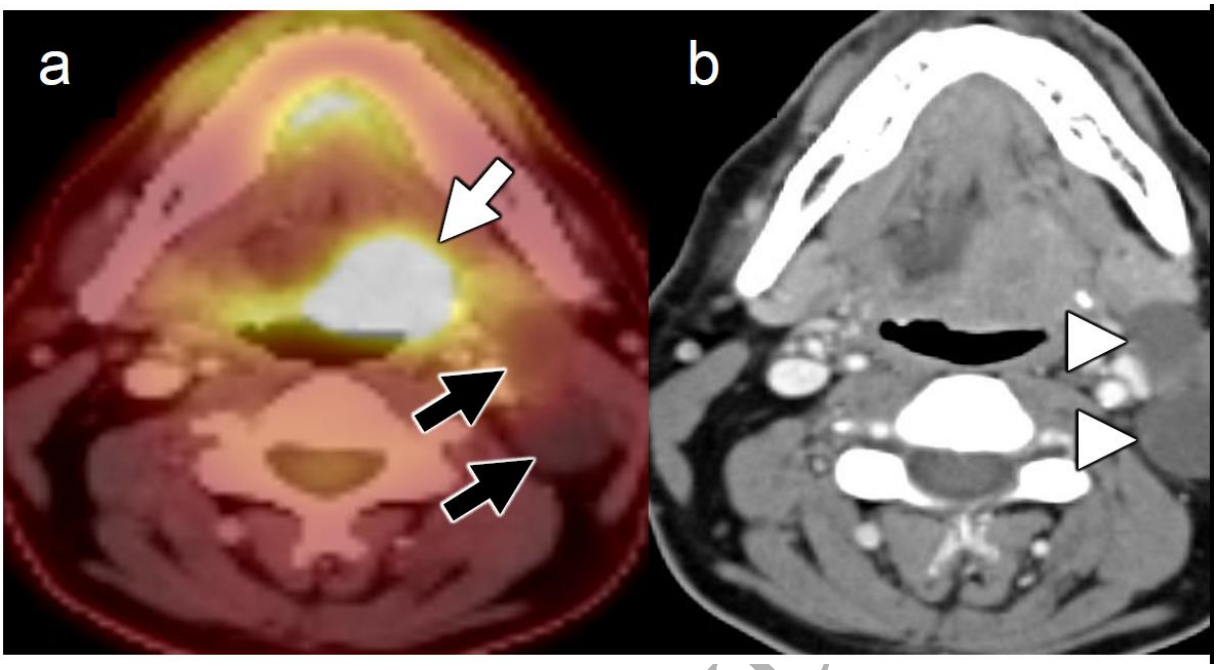

Figure 10. False negative FDG/PET due to necrotic lymph nodes. Fused axial FDG-PET/CT (a) in a patient with left base of tongue squamous cell carcinoma (white arrow) shows two non-FDG avid masses in the left suprahyoid neck (black arrows). Corresponding axial CECT (b) shows these necrotic level II lymph nodes (white arrowheads) to be low density (fluid attenuation). Because of necrosis, these nodes do not have sufficient metabolic activity to register FDG uptake and are an important pitfall in head and neck oncologic imaging.

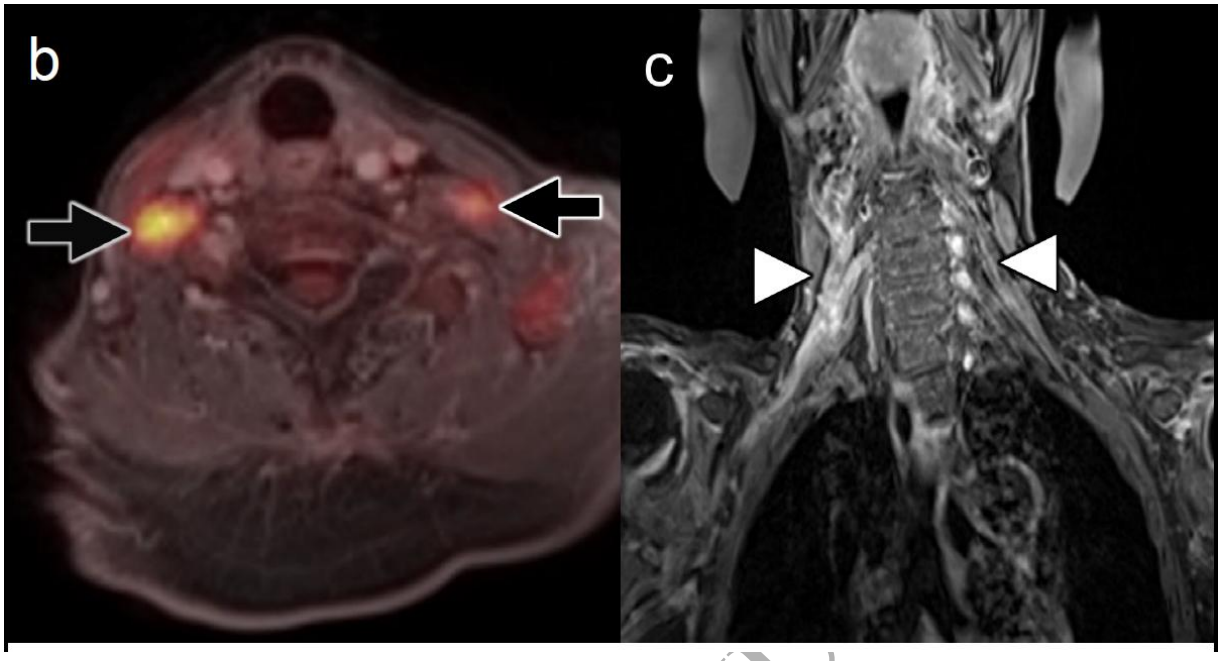

Figure 11. Misleading near-symmetric FDG uptake. Fused coronal FDG-PET/MRI (T1-weighted pre-contrast image) (a) in a patient with biopsy-proven neurolymphomatosis shows bilateral FDG uptake in the brachial plexus (white arrows). Fused axial FDG-PET/MRI (T1-weighted post-contrast fat-saturated image) (b) shows the bilateral FDG uptake within the brachial plexus (black arrows) to be mildly greater on the right. Coronal T1 Dixon post-contrast fast-saturated MRI (c) shows marked enhancement (white arrowheads) of the enlarged (right greater than left) brachial plexus nerve roots. Axial DWI trace (d) shows markedly hyperintense brachial plexus (black arrowheads) bilaterally due to a combination of high cellularity lymphomatous infiltrate and intrinsic fractional anisotropy of the brachial plexus resulting in reduced diffusivity. This case shows the risk in assuming that “symmetry is your friend”; rather, symmetry may be your “frenemy”!